

U.S.S.N. 10/003,983

Filed: October 31, 2001

AMENDMENT AND RESPONSE TO OFFICE ACTION

In the Claims

1. (Canceled).
2. (Currently Amended) A peptide according to ~~Claim 1~~ of 9 to 12 amino acid residues, wherein the peptide comprises at least one an HLA-binding peptide of the human CD45 polypeptide comprising the amino acid sequence selected from the group consisting of FLYDVIAST (SEQ ID NO:1), ~~ALLAFLAFL (SEQ ID NO:2), KLFTAKLNV (SEQ ID NO:3), MIWEQKATV (SEQ ID NO:4), NLSELHPYL (SEQ ID NO:5), VNLSLHPYL (SEQ ID NO:6), LLAFGFAFL (SEQ ID NO:7), YLYNKETKL (SEQ ID NO:8), LILDVPPGV (SEQ ID NO:9), TLILDVPPGV (SEQ ID NO:10), ILYNNHKFT (SEQ ID NO:11), ILPYDYNRV (SEQ ID NO:12), YILHIQALV (SEQ ID NO:13), FQLHDTQV (SEQ ID NO:14), KLLAFGFAFL (SEQ ID NO:15), YQYQYTNWSV (SEQ ID NO:16), and portions and variants of any of these~~ or a variant of SEQ ID NO:1, wherein the variant contains one or two amino acid substitutions at positions 2 and 9.
3. (Currently Amended) A peptide according to Claim 1 ~~2~~ wherein the peptide ~~or the said portion or variant thereof~~ is capable of binding to HLA-A0201.
4. (Currently Amended) A peptide according to Claim 3 wherein when bound to HLA-A0201 the peptide-bound HLA-A0201 is capable of eliciting the production of a cytotoxic T lymphocyte (CTL) which recognizes a cell which expresses a polypeptide comprising the ~~given amino acid sequence~~ the HLA-binding peptide of human CD45 polypeptide.
5. (Currently Amended, Withdrawn) A peptide according to Claim 1 ~~2~~ wherein the peptide includes non-peptide bonds.

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6. (Currently Amended) A peptide according to Claim 2 comprising ~~at least one the~~ amino acid sequence ~~selected from the group consisting of~~ FLYDVIAST (SEQ ID NO:1); ALIAFLAFL (SEQ ID NO:2); KLFTAKLNV (SEQ ID NO:3); MIWEQKATV (SEQ ID NO:4); NLSELHPYL (SEQ ID NO:5); VNLSELHPYL (SEQ ID NO:6); LLAFGFAFL (SEQ ID NO:7); YLYNKETKL (SEQ ID NO:8); LILDVPPGV (SEQ ID NO:9); TLILDVPPGV (SEQ ID NO:10); ILYNNHKFT (SEQ ID NO:11); ILPYDYNRV (SEQ ID NO:12); YLIIQALV (SEQ ID NO:13); FQLHIDCTQV (SEQ ID NO:14); KLLAFGFAFL (SEQ ID NO:15); and XQYQYTNSWV (SEQ ID NO:16).

7. (Canceled).

8. (Currently Amended, Withdrawn) A polynucleotide encoding a peptide according to Claim ~~1~~ 2 or fusion molecule thereof which comprises an HLA heavy chain molecule joined via a flexible linker to an HLA-binding peptide of CD45 such that the HLA-binding peptide is able to occupy the peptide-binding groove of the HLA molecule.

9. (Withdrawn) A polynucleotide according to Claim 8 which is DNA.

10. (Withdrawn) The polynucleotide according to Claim 8 further comprising an expression vector capable of expressing the peptide.

11. (Withdrawn) A host cell comprising a polynucleotide according to Claim 8 alone or in an expression vector.

12. (Currently Amended, Withdrawn) A method of producing a peptide according to Claim ~~1~~ 2 or fusion molecule thereof which comprises an HLA heavy chain molecule joined via a flexible linker to an HLA-binding peptide of CD45 such that the HLA-binding peptide is able

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to occupy the peptide-binding groove of the HLA molecule comprising culturing the host cell according to Claim 11 and obtaining the peptide from the host cell or its culture medium.

13. (Currently Amended, Withdrawn) A kit of parts comprising a peptide according to Claim ~~1~~ 2 and antigen presenting cell.

14. (Withdrawn) A kit of parts according to Claim 13 wherein the antigen presenting cell is a cell defective in, or lacks, the expression of the TAP peptide transporter.

15. (Withdrawn) A kit of parts according to Claim 14 wherein the cell is any one of the T2 cell, an RMA-S cell or a *Drosophila* cell.

16. (Currently Amended, Withdrawn) An antigen-presenting cell wherein its MHC Class I molecules are loaded with a peptide according to Claim ~~1~~ 2.

17. (Withdrawn) A cell according to Claim 16 which is defective in, or lacks, the expression of the TAP peptide transporter.

18. (Withdrawn) A cell according to Claim 17 selected from the group consisting of a T2 cell, an RMA-S cell and a *Drosophila* cell.

19. (Currently Amended, Withdrawn) A method for producing activated cytotoxic T lymphocytes (CTL) *in vitro*, the method comprising contacting *in vitro* CTL, which antigen-loaded human class I MHC molecules expressed on the surface of a suitable antigen-presenting cell for a period of time sufficient to activate, in an antigen specific manner, said CTL, wherein the antigen is a peptide according to Claim ~~1~~ 2.

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20. (Withdrawn) A method according to Claim 19 wherein the CTL and the antigen-presenting cell are allogeneic with respect to the class I MHC molecule that is presenting peptides of CD45.

21. (Withdrawn) A method according to Claim 19 wherein the antigen is loaded onto class I MHC molecules expressed on the surface of a suitable antigen-presenting cell by contacting a sufficient amount of the antigen with an antigen presenting cell wherein before contact the class I MHC molecules of the antigen-presenting cell are substantially unoccupied and after contact the class I MHC molecules are substantially fully occupied.

22. (Withdrawn) A method according to claim 19 wherein the antigen-presenting cell comprises an expression vector which expresses a peptide according to Claim 10.

23. (Withdrawn) A method to any one of Claim 19 wherein the class I MHC molecule in HLA-A0201.

24. (Withdrawn) Activated cytotoxic T lymphocytes (CTL) obtainable by the method according to Claim 19.

25. (Currently Amended, Withdrawn) Activated cytotoxic T lymphocytes (CTL) which selectively recognise a cell which expresses a polypeptide comprising an amino acid sequence given in Claim ~~1~~2.

26. (Withdrawn) Activated cytotoxic T lymphocytes (CTL) which selectively recognise a malignant cell which expresses CD45.

27. (Currently Amended, Withdrawn) A T-cell receptor (TCR) which recognises a cell which expresses a polypeptide comprising an amino acid sequence given in Claim ~~1~~2.

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28. (Withdrawn) A T-cell receptor (TCR) or a functionally equivalent molecule to the TCR which recognises a malignant haematopoietic which expresses CD45.

29. (Currently Amended, Withdrawn) A polynucleotide encoding a T cell receptor (TCR) selected from the group consisting of a T-cell receptor (TCR) which recognises a cell which expresses a polypeptide comprising an amino acid sequence given in Claim 12 and a T-cell receptor (TCR) or a functionally equivalent molecule to the TCR which recognises a malignant haematopoietic which expresses CD45

30. (Currently Amended, Withdrawn) An expression vector capable of expressing a T cell receptor (TCR) selected from the group consisting of a T-cell receptor (TCR) which recognises a cell which expresses a polypeptide comprising an amino acid sequence given in Claim 12 and a T-cell receptor (TCR) or a functionally equivalent molecule to the TCR which recognises a malignant haematopoietic which expresses CD45.

31. (Currently Amended, Withdrawn) A method of killing target cells in a patient which target cells express a polypeptide comprising an amino acid sequence given in Claim 12, the method comprising administering to the patient an effective number of cytotoxic T lymphocytes (CTL) selected from the group consisting of activated cytotoxic T lymphocytes (CTL) obtainable by the method according to Claim 19, activated cytotoxic T lymphocytes (CTL) which selectively recognise a cell which expresses a polypeptide comprising an amino acid sequence given in Claim 12, and activated cytotoxic T lymphocytes (CTL) which selectively recognise a malignant cell which expresses CD45.

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32. (Withdrawn) A method according to Claim 31 wherein the patient has undergone an allogeneic stem cell transplantation.

33. (Withdrawn) A method According to Claim 31 wherein the target cells are cancer cells.

34. (Withdrawn) A method according to Claim 33 wherein the cancer is a leukaemia which expresses the CD45 polypeptide.

35. (Withdrawn) A method of treating a patient with a haematopoietic malignancy, the method comprising (1) determining for a given HLA-binding peptide of human CD45 which type of Class I MHC molecule binds the peptide in a patient, or determining for a given Class I MHC molecule of the patient which peptide (or peptides) of human CD45 binds the Class I MHC molecule in the patient, or both, (2) providing an activated CTL which is allogeneic (allorestricted) with respect to the Class I MHC molecule which binds the peptide in the patient and which CTL is specific for the peptide, (3) undertaking a stem cell transplantation of the patient from a donor who is negative for the type of Class I MHC molecule which, in the patient, binds the peptide, and (4) administering the activated CTL of step (2) to the patient.

36. (Withdrawn) A method according to Claim 35 wherein the type of Class I MHC molecule is determined by DNA analysis.

37. (Withdrawn) A method according to Claim 35 wherein in step (2) the activated CTL are produced by the method of Claim 19 wherein the CTL are allogenic (allorestricted) with respect to the Class I MHC molecule which presents the peptide in the patient.

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38. (Withdrawn) A method according to Claim 35 wherein in step (2) the activated CTL are selected from a library of CTL.

39. (Withdrawn) A library of activated CTL wherein each member of the library (1) recognises a CD45 peptide when presented by a particular, recorded HLA and (2) has its HLA haplotype recorded.

40. (Withdrawn) A library of HLA-binding peptides of human CD45 polypeptide wherein for each member of the library the type of HLA molecule it binds is recorded.

41. (Withdrawn) A library of antigen presenting cells each loaded with an HLA-binding peptide of human CD45 polypeptide wherein for each member of the library the identity of the peptide is recorded and, optionally, the HLA haplotype of the antigen presenting cell.

42. (New) The peptide of claim 2 wherein the peptide is FLYDVIAST (SEQ ID NO:1).